Page 5 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

## **CLAIM AMENDMENTS**

RECEIVED CENTRAL FAX CENTER NOV 2.7 2006

Claim 1. (Currently Amended) A compound of formula I

or pharmaceutically acceptable salts and prodrugs thereof, wherein

A is selected from the group consisting of a covalent bond, CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>;

B is selected from the group consisting of CH<sub>2</sub> and CH<sub>2</sub>CH<sub>2</sub>, provided that when A is CH<sub>2</sub>CH<sub>2</sub>, then B is CH<sub>2</sub>;

Y is selected from the group consisting of a covalent bond, CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>;

Z is selected from the group consisting of a covalent bond, CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>, provided that when Y is CH<sub>2</sub>CH<sub>2</sub>, then Z is a covalent bond and further provided that when Z is CH<sub>2</sub>CH<sub>2</sub>, then Y is a covalent bond;

R<sub>1</sub> is selected from the group consisting of

Page 6 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

R<sub>3</sub> is selected from the group consisting of hydrogen, alkyl, and halogen;

R<sub>4</sub> is selected from the group consisting of hydrogen, alkoxy, alkyl, amino, halogen, and nitro;

 $R_5$  is selected from the group consisting of hydrogen, alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonyloxy, alkylthio, alkynyl, amino, aminoalkyl, aminocarbonyl, aminocarbonylalkyl, aminosulfonyl, carboxy, carboxyalkyl, cyano, cyanoalkyl, formyl, formylalkyl, haloalkoxy, haloalkyl, halogen, hydroxy, hydroxyalkyl, mercapto, mercaptoalkyl, nitro, 5-tetrazolyl, -NR $_6$ S(O) $_2$ R $_7$ , -C(NR $_6$ )NR $_7$ R $_8$ , -CH $_2$ C(NR $_6$ )NR $_7$ R $_8$ , -C(NOR $_6$ )R $_7$ , -C(NCN)R $_6$ , -C(NNR $_6$ R $_7$ )R $_8$ , -S(O) $_2$ OR $_6$ , and -S(O) $_2$ R $_6$ ;

 $R_6$ ,  $R_7$ , and  $R_8$  are independently selected from the group consisting of hydrogen and alkyl; and

R<sub>9</sub> is selected from the group consisting of hydrogen, alkoxycarbonyl, alkyl, amino, aminoalkyl, aminocarbonylalkyl, benzyloxycarbonyl, cyanoalkyl, dihydro-3-pyridinylcarbonyl, hydroxy, hydroxyalkyl, and phenoxycarbonyl.

Page 7 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

## Claim 2. (Original) A compound according to claim 1 wherein

R<sub>1</sub> is selected from the group consisting of

and

Claim 3. (Withdrawn) A compound according to claim 1 of formula II

or pharmaceutically acceptable salts and prodrugs-thereof.

Claim 4. (Withdrawn) A compound according to claim 3 wherein Y is a covalent bond and Z is  $CH_2$ .

## Claim 5. (Withdrawn) A compound according to claim 3 wherein

Y is a covalent bond;

Z is CH2; and

 $R_1$  is

$$R_3$$
  $R_4$ 

Page 8 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

## Claim 6. (Withdrawn) A compound according to claim 5 selected from the group consisting of

(cis)-6-(3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(cis)-6-(6-chloro-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1R,5S)-6-(3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1R,5S)-6-(5-bromo-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(6-chloro-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1R,5S)-6-(6-chloro-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(5-ethynyl-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(5-vinyl-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

5-[(1S,5R)-3,6-diazabicyclo[3.2.0]hept-6-yl]nicotinonitrile;

(-) (cis)-6-(5-bromo-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(cis)-6-(5-bromo-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(6-bromo-5-vinyl-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

2-bromo-5-[(1R,5S)-3,6-diazabicyclo[3.2.0]hept-6-yl]nicotinonitrile;

(1R,5S)-6-(5-ethynyl-3-pyridinyl)-3,6-diazabicyclo[3,2,0]heptane;

(1R,5S)-6-(5,6-dichloro-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(5,6-dichloro-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(cis)-6-(5,6-dichloro-3-pyridinyl)-3,6-diazabicyclo[3,2,0]heptane;

(1R,5S)-6-(5-methoxy-3-pyridinyl)-3,6-diazabicyclo[3,2.0]heptane;

(1S,5R)-6-(5-methoxy-3-pyridinyl)-3,6-diazabicyclo[3,2,0]heptane;

(cis)-6-(6-bromo-5-methoxy-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1R,5S)-6-(6-chloro-5-methyl-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

(1S,5R)-6-(6-chloro-5-methyl-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane;

Page 9 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

(cis)-6-(6-chloro-5-methyl-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane; (1R,5S)-6-(6-bromo-5-methoxy-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane; (1S,5R)-6-(6-bromo-5-methoxy-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane; (cis)-6-(5-azido-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane; (1R,5S)-6-(5-azido-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane; and (1R,5S)-6-(5-azido-3-pyridinyl)-3,6-diazabicyclo[3.2.0]heptane.

Claim 7. (Withdrawn) A compound according to claim 5 that is 5-[(1R,5S)-3,6-diazabicyclo[3.2.0]hept-6-yl]nicotinonitrile.

Claim 8. (Withdrawn) A compound according to claim 3 wherein Y is CH<sub>2</sub> and Z is a covalent bond.

Claim 9. (Withdrawn) A compound according to claim 3 wherein

Y is CH2:

Z is a covalent bond; and

 $R_1$  is

Claim 10. (Withdrawn) A compound according to claim 9 selected from the group consisting of

(1R,5R)-6-(6-chloro-3-pyridinyl)-2,6-diazabicyclo[3.2.0]heptane and (1R,5R)-6-(3-pyridinyl)-2,6-diazabicyclo[3.2.0]heptane.

Claim 11. (Withdrawn) A compound according to claim 3 wherein Y is CH<sub>2</sub>CH<sub>2</sub> and Z is a covalent bond.

Page 10 of 20 USSN 10/810,999 6696,US.D1 Response to Office Action

Claim 12. (Withdrawn) A compound according to claim 3 wherein Y is CH<sub>2</sub> and Z is CH<sub>2</sub>.

Claim 13. (Withdrawn) A compound according to claim 3 wherein Y is a covalent bond and Z is CH<sub>2</sub>CH<sub>2</sub>.

Claim 14. (Withdrawn) A compound according to claim 3 wherein

Y is a covalent bond;

Z is CH2CH2; and

 $R_1$  is

Claim 15. (Withdrawn) A compound according to claim 14 selected from the group consisting of

(cis)-8-(3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(cis)-8-(6-chloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1S,6R)-(cis)-8-(6-chloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(-) (cis)-8-(6-chloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

5-[(1R,6S)-3,8-diazabicyclo[4.2.0]oct-8-yl]nicotinonitrile;

(1S,6R)-5-[3,8-diazabicyclo[4.2.0]oct-8-yl]nicotinonitrile;

(1S,6R)-8-(5-methoxy-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(cis)-8-(5-methoxy-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1R,6S)-8-(5-methoxy-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(cis)-8-(6-chloro-5-methyl-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1S,6R)-8-(6-chloro-5-methyl-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

Page 11 of 20 USSN 10/810,999 6696,US.D1 Response to Office Action

(1R,6S)-8-(6-chloro-5-methyl-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1S,6R)-8-(3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1R,6S)-8-(3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(cis)-8-(5,6-dichloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1S,6R)-8-(5,6-dichloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane; and

(1R,6S)-8-(5,6-dichloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane.

Claim 16. (Currently Amended) A compound according to claim 1 of formula III

Ш,

or pharmaceutically acceptable salts and prodrugs thereof.

Claim 17. (Original) A compound according to claim 16 wherein Y is a covalent bond and Z is a covalent bond.

Claim 18. (Original) A compound according to claim 16 wherein

Y is a covalent bond:

Z is a covalent bond; and

R<sub>1</sub> is

$$R_3$$
  $R_4$ 

Claim 19. (Original) A compound according to claim 18 that is (1R,5R)-2-(3-pyridinyl)-2,6-diazabicyclo[3.2.0]heptane.

Page 12 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 20. (Original) A compound according to claim 16 wherein Y is CH<sub>2</sub> and Z is a covalent bond.

Claim 21. (Original) A compound according to claim 16 wherein Y is a covalent bond and Z is CH<sub>2</sub>.

Claim 22. (Original) A compound according to claim 16 wherein

Y is a covalent bond;

Z is CH2; and

R<sub>1</sub> is

Claim 23. (Original) A compound according to claim 22 selected from the group consisting of

(cis)-1-(6-chloro-3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole;

(cis)-1-(6-chloro-3-pyridinyl)-5-methyloctahydropyrrolo[3,4-b]pyrrole;

(3aR,6aR)-1-(6-chloro-3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole;

(3aR,6aR)-1-(3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole;

(3aS,6aS)-1-(6-chloro-3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole;

(3aS,6aS)-1-(3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole;

5-((3aR,6aR)-hexahydropyrrolo[3,4-b]pyrrol-1(2H)-yl)nicotinonitrile;

(3aS,6aS)-1-(5-hydroxy-3-pyridinyl) octahydropyrrolo[3,4-b]pyrrole; and

 $5\hbox{-}((3aS,6aS)\hbox{-}hexahydropyrrolo[3,4\hbox{-}b]pyrrol\hbox{-}1(2H)\hbox{-}yl)nicotinonitrile.$ 

Pags 13 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 24. (Original) A compound according to claim 16 wherein Y is CH<sub>2</sub>CH<sub>2</sub> and Z is a covalent bond.

Claim 25. (Original) A compound according to claim 16 wherein Y is  $CH_2$  and Z is  $CH_2$ .

Claim 26. (Original) A compound according to claim 16 wherein Y is a covalent bond and Z is  $CH_2CH_2$ .

Claim 27. (Canceled)

Claim 28. (Canceled)

Claim 29. (Canceled)

Claim 30. (Canceled)

Claim 31. (Canceled)

Claim 32. (Canceled)

Claim 33. (Canceled)

Claim 34. (Canceled)

Claim 35. (Canceled)

Page 14 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 36. (Canceled)

Claim 37. (Canceled)

Claim 38. (Canceled)

Claim 39. (Canceled)

Claim 40. (Canceled)

Claim 41. (Withdrawn) A compound according to claim 1 of formula V

or pharmaceutically acceptable salts and prodrugs thereof.

Claim 42. (Withdrawn) A compound according to claim 41 wherein Y is a covalent bond and Z is a covalent bond.

Claim 43. (Withdrawn) A compound according to claim 41 wherein Y is CH<sub>2</sub> and Z is a covalent bond.

Claim 44. (Withdrawn) A compound according to claim 41 wherein Y is a covalent bond and Z is CH<sub>2</sub>.

Page 15 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 45. (Withdrawn) A compound according to claim 41 wherein Y is CH2CH<sub>2</sub> and Z is a covalent bond.

Claim 46. (Withdrawn) A compound according to claim 41 wherein Y is  $CH_2$  and Z is  $CH_2$ .

Claim 47. (Withdrawn) A compound according to claim 41 wherein Y is a covalent bond and Z is  $CH_2CH_2$ .

Claim 48. (Withdrawn) A compound according to claim 1 of formula VI

VI,

or pharmaceutically acceptable salts and prodrugs thereof.

Claim 49. (Withdrawn) A compound according to claim 48 wherein Y is a covalent bond and Z is a covalent bond.

Claim 50. (Withdrawn) A compound according to claim 48 wherein Y is CH<sub>2</sub> and Z is a covalent bond.

Claim 51. (Withdrawn) A compound according to claim 48 wherein Y is a covalent bond and Z is CH<sub>2</sub>.

Claim 52. (Withdrawn) A compound according to claim 48 wherein Y is CH<sub>2</sub>CH<sub>2</sub> and Z is a covalent bond.

Claim 53. (Withdrawn) A compound according to claim 48 wherein Y is  $CH_2$  and Z is  $CH_2$ .

Page 16 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 54. (Withdrawn) A compound according to claim 48 wherein Y is a covalent bond and Z is  $CH_2CH_2$ .

Claim 55. (Withdrawn) A compound according to claim 1 of formula VII

VII.

or pharmaceutically acceptable salts and prodrugs thereof.

Claim 56. (Withdrawn) A compound according to claim 55 wherein Y is a covalent bond and Z is a covalent bond.

Claim 57. (Withdrawn) A compound according to claim 55 wherein

Y is a covalent bond;

Z is a covalent bond; and

R<sub>i</sub> is

Claim 58. (Withdrawn) A compound according to claim 57 selected from the group consisting of

(cis)-3-(3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(cis)-3-(6-chloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane;

(1R,6S)-3-(6-chloro-3-pyridinyl)-3,8-diazabicyclo[4.2.0]octane; and

(cis)-5-[3,8-diazabicyclo[4.2.0]oct-3-yl]nicotinonitrile.

Page 17 of 20 USSN 10/810,999 6696,US.D1 Response to Office Action

Claim 59. (Withdrawn) A compound according to claim 55 wherein Y is  $CH_2$  and Z is a covalent bond.

Claim 60. (Withdrawn) A compound according to claim 55 wherein

Y is a covalent bond;

Z is a covalent bond; and

R<sub>1</sub> is

Claim 61. (Withdrawn) A compound according to claim 60 that is (cis)-6-(3-pyridinyl)octahydro-1H-pyrrolo[2,3-c]pyridine.

Claim 62. (Withdrawn) A compound according to claim 55 wherein Y is CH<sub>2</sub>CH<sub>2</sub> and Z is a covalent bond.

Claim 63. (Withdrawn) A compound according to claim 1 of formula VIII

VIII,

or pharmaceutically acceptable salts and prodrugs thereof.

Claim 64. (Withdrawn) A compound according to claim 63 wherein Y is a covalent bond and Z is a covalent bond.

Page 18 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 65. (Withdrawn) A compound according to claim 63 wherein Y is CH<sub>2</sub> and Z is a covalent bond.

Claim 66. (Withdrawn) A compound according to claim 63 wherein Y is a covalent bond and Z is  $CH_2$ .

Claim 67. (Withdrawn) A compound according to claim 1 of formula IX

IX.

or pharmaceutically acceptable salts and prodrugs thereof.

Claim 68. (Withdrawn) A compound according to claim 67 wherein Y is a covalent bond and Z is a covalent bond.

Claim 69. (Withdrawn) A compound according to claim 67 wherein Y is CH<sub>2</sub> and Z is a covalent bond.

Claim 70. (Withdrawn) A compound according to claim 67 wherein Y is a covalent bond and Z is  $CH_2$ .

Claim 71. (Original) A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a pharmaceutically acceptable carrier.

Claim 72. (Canceled)

Claim 73. (Currently Amended) A method of treating a disorder wherein the disorder is ameliorated by controlling neurotransmitter release in a host mammal in need of such

Page 19 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

treatment, comprising administering a therapeutically effective amount of a compound of Claim 1, wherein the disorder is selected from the group consisting of Alzheimer's disease, Parkinson's disease, memory dysfunction, Tourette's syndrome, sleep disorders, attention deficit hyperactivity disorder, neurodegeneration, inflammation, neuroprotection, amyotrophic lateral sclerosis, anxiety depression, mania, schizophrenia, eating disorders, AIDS-induced dementia, epilepsy, urinary incontinence, Crohn's disease, migraines, pain, PMS, erectile dysfunction, substance abuse, smoking cessation, and inflammatory bowel syndrome.

Claim 74. (Original) The method of claim 73 wherein the disorder is selected from the group consisting of Alzheimer's disease, Parkinson's disease, attention deficit hyperactivity disorder, depression, nicotinic withdrawal syndrome, Tourette's syndrome, and schizophrenia.

Claim 75. (Original) The method of claim 73 wherein the disorder is pain.

Claim 76. (Original) A method of treating pain in a mammal comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1 in combination with a non-steroid anti-inflammatory agent and a pharmaceutically acceptable carrier.

Claim 77. (Original) A method of treating pain in a mammal comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1 in combination with an opioid and a pharmaceutically acceptable carrier.

Claim 78. (Original) A method of treating pain in a mammal comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1 in combination with a tricyclic antidepressant and a pharmaceutically acceptable carrier.

Claim 79. (Original) A method of treating pain in a mammal comprising administering to a mammal in need of such treatment a therapeutically effective amount of a compound of Claim 1 in combination with an anticonvulsant and a pharmaceutically acceptable carrier.

Page 20 of 20 USSN 10/810,999 6696.US.D1 Response to Office Action

Claim 80. (NEW) A compound that is (3aR,6aR)-1-(3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole or a salt thereof.

Claim 81. (NEW) A pharmaceutical composition comprising a therapeutically effective amount of a compound of (3aR,6aR)-1-(3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole in combination with a pharmaceutically acceptable carrier.

Claim 82. (NEW) A method of treating a disorder in a mammal in need of such treatment, comprising administering a therapeutically effective amount of (3aR,6aR)-1-(3-pyridinyl)octahydropyrrolo[3,4-b]pyrrole, wherein the disorder is selected from the group consisting of Alzheimer's disease, Parkinson's disease, memory dysfunction, Tourette's syndrome, sleep disorders, attention deficit hyperactivity disorder, neurodegeneration, inflammation, neuroprotection, amyotrophic lateral sclerosis, anxiety depression, mania, schizophrenia, eating disorders, AIDS-induced dementia, epilepsy, urinary incontinence, Crohn's disease, migraines, pain, PMS, erectile dysfunction, substance abuse, smoking cessation, and inflammatory bowel syndrome